A Comparison Pilot Study of Motor-level Electrical Stimulations for Lowering Postprandial Glucose Levels

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Abstract

Purpose: The purpose of this study is to compare the effects of three Motor-level Electrical Stimulation (MES) parameters, NMES, Russian current, and low-rate transcutaneous electric nerve stimulation (TENS) on non-diabetic healthy subjects' postprandial glucose levels, heart rate, and oxygen consumption (VO2).

Background: MES has been shown to improve glucose tolerance and glucose uptake in both animals and humans. The effects of MES include increasing the following: heart rate, blood pressure, oxygen uptake, ventilatory capacity, muscle bulk, muscle oxidative process, and muscle glycogen depletion. Recently, MES has been shown to improve blood glucose control in people with type 2 diabetes. However, limited research is available that comprehensively compares varying MES parameters on the effects of postprandial glucose levels.

Methods: Twenty-eight healthy student subjects were randomly assigned to either the NMES, Russian current, TENS, or control group without any MES. Subjects participated in an overnight fast of at least 8 hours and had their fasting blood glucose measured. Subjects were given a glucose supplement to drink within 10 minutes, rested in supine for 30 minutes then the second glucose level was taken. Subjects received a 30 minute treatment intervention followed by the third blood glucose measurement. Subjects then rested an additional 30 minutes followed by obtaining the final blood glucose measurement. VO2 levels were monitored every 30 seconds, and heart rate was monitored every 3 minutes throughout the 90 minute study.

Results: There were no significant differences between groups on glucose levels and heart rates throughout the study. The Russian group demonstrated a statistically significant increase up to 10% in VO2 compared to the control group.

Conclusion: MES seems to have no effects on postprandial glucose levels in non-diabetic healthy subjects. While 30-minute MES treatment did not change the heart rate, Russian current significantly increased the VO2. Our findings indicate Russian current may have the potential to be applied to mimic exercise better than NMES or TENS. Further research is required to explore the effects of Russian current on blood glucose levels in people with T2D.

Introduction

Diabetes is a chronic disease marked by high blood glucose levels. It is characterized by impairment of insulin production (from the islet cells in the pancreas), insulin action (to help the body in utilizing blood glucose), or both. According to the CDC's 2014 National Diabetes Statistics Report, nearly 29.1 million people (9.3% of the population) in the United States have diabetes. It is estimated that as many as 1 in 3 American adults will have diabetes by 2050 (1). Type 2 Diabetes (T2D) accounts for approximately 90-95% of all diagnosed cases of diabetes. It results from insulin resistance, a disorder in which muscle cells and fat cells fail to respond normally to insulin, leading to high blood glucose levels.

Exercise has been suggested as an effective treatment to improve blood glucose control for people with T2D (2-6). Research has shown that exercise can improve glucose uptake into skeletal muscle in patients with T2D (6). However, many patients with T2D are physically restricted from the recommended exercise because of excessive obesity, orthopedic diseases, neurological diseases, chronic illness, or prolonged periods of being bedridden. Therefore, individuals such as these who cannot receive the benefit of exercise remain exposed to the risk of diabetic complications such as stroke, heart disease, kidney failure, blindness, amputation, and premature death.

Motor-level electrical stimulation (MES) is one of the modalities used in physical therapy clinics that induces involuntary contraction of skeletal muscle simultaneously for different strengthening and rehabilitation purposes. MES has been suggested to mimic voluntary exercise in patients with neuromuscular disorders. The benefits include increasing heart rate, blood pressure, oxygen uptake, ventilatory capacity, muscle bulk, muscle oxidative processes, and muscle glycogen depletion (7-10). More specifically, MES improves glucose tolerance and glucose uptake in both animals (11-14) and humans (15-19). Recently, it has been reported that a 30-minute single bout of MES significantly attenuated postprandial glucose levels in middle-aged men with metabolic syndrome (20) and patients with T2D (21, 22). One recent study published in 2015 also suggests that a 10-week MES treatment (twice weekly for 20 minutes) can improve glucose metabolism and functional performance in patients with T2D (23). In summary, all these findings indicate that MES might emerge as a novel intervention for controlling glucose levels in those patients with T2D who cannot perform adequate voluntary exercise.

In physical therapy clinics, several types of MES are available based on different parameters. For example, NMES, Russian current, and low-rate transcutaneous electric nerve stimulation (TENS) are the most common protocols that simultaneously produce skeletal muscle contraction. However, it is unclear which MES parameters best mimic exercise for controlling glucose levels in people with T2D.

In this preliminary study, we compared the postprandial glucose levels, heart rates, and oxygen consumption (VO2) by applying three types of MES as described above on non-diabetic healthy subjects. We hypothesized that the subjects who received a 30-minute single bout of MES would have a better outcome in decreasing postprandial glucose levels when compared to the controls. The objective was to determine the optimal type of MES to mimic an effective exercise for postprandial skeletal muscle glucose uptake.

Methods

Subjects

The study protocol was approved by the IRB of Angelo State University (HUA-040115). Twenty-eight healthy student subjects were recruited from Angelo State University. The inclusion criteria were: currently healthy, able to follow verbal commands or instructions, able to read and fill out a subject intake form, able to fast for 8 hours, and body weight more than 94 lbs. The exclusion criteria were: diabetes diagnosis, infectious diseases, currently taking any blood thinning medications, presence of a blood clotting disorder, fear/aversion of finger pricked, fear/aversion of electrical stimulation, presence of cardiac pacemaker, pregnancy, venous/arterial thrombosis, cardiac disease, malignant tumor, impaired mentation, and impaired sensation. The subjects were randomly assigned into one of four groups: 1) NMES, 2) Russian current, 3) Low-rate TENS, and 4) Control group. The physical characteristics of the subjects in each group were summarized in Table 1. No significant differences were found among subjects.

Postprandial glucose levels measurement

The entire procedure of this study was summarized in Figure 1. Briefly, each subject arrived at the Human Performance Lab in the Department of Physical Therapy at Angelo State University the morning after having completed an overnight fast for at least 8 hours. They verbally confirmed criteria guidelines, signed consent forms, and completed the health intake form. The subjects had their vital signs (heart rate and blood pressure; Carescape V100 Monitor, GE Healthcare) and their first fasting blood glucose level measured by the equipment manufacturer's directions (Glucose meter: ACCU-CHEK® Nano; Glucose test strips: ACCU-CHEK® SmartView; Lancets: ACCU-CHEK® Softclix). After measuring the baseline glucose level, a glucose supplement, Trutol™ 75g (Thermo Fisher Scientific, Inc.) was given to each subject to drink within a 10 minute time frame. After the allotted drinking period, the subjects were positioned supine on a treatment table. Thirty minutes after finishing the supplement, the second blood glucose level was measured (as the first postprandial glucose level) followed by the onset of electrical stimulation. The subjects in the control group received the identical MES setup as other groups, but they did not receive any output of electrical currents. After the 30-minute of allotted MES, treatment was terminated and the subjects had their third blood glucose level measured (as the second postprandial glucose level). The participants remained in a supine position and rested for an additional 30 minutes on the treatment table. Following the final rest period, the participants had their final blood glucose level measured (as the third postprandial glucose level). Finally, the subjects were dismissed after checking their vital signs.

Electrical stimulation protocol

Thirty minutes after drinking the glucose supplement, electrical stimulation (Dynatron Solaris® 709) was applied to the subjects' thighs for 30 minutes, excluding the control group. The control group had the identical electrode setup as the treatment groups, but they did not receive electrical currents. Four pairs of 2 in x 4 in rectangular electrodes (Dynatronics™, 7B0284-CS Ultra Polys™) were applied to each subject's bilateral thighs (Figure 2). The target muscles on the thighs were the bilateral quadriceps and bilateral hamstrings. The electrode placement for the quadriceps was: proximal electrode- 15 cm distal from ASIS and lateral to the sartorius; distal electrode- medial to the sartorius and 10 cm proximal from femoral epicondyle. The electrode placement for the hamstrings was: medial and lateral hamstrings; 5 cm distal to ischial tuberosity; 5 cm between the two electrodes. The parameters for pulse duration and frequency/rate for each group were summarized in Table 2. All three MES treatments included a duty cycle with a 3-second on and 3-second off phase. These parameters have been selected based upon average values and with an effort to ensure significantly different parameters from one treatment method to another (24). The 30-minute time period was chosen based on the literatures (21, 22). MES was administered for 30 minutes at the participant's tolerance level. The current intensity was adjusted every 10 minutes based on the participants' tolerances.

Oxygen consumption measurement and heart rate monitor

The entirety of this study was completed in a noise-controlled, comfortable, and low lit environment. Maximal relaxation was targeted in order to obtain the most accurate measurement of resting oxygen consumption. Patients were instructed to relax with limited movement and prohibited from other activities such as reading, talking, listening to music or other stimulating/engaging tasks.

The oxygen consumption and heart rate were measured throughout the study for 90 minutes (Figure 3). The VO_2 was calculated every 30 seconds and securely stored using COSMED Quark CPET software. Heart rate was monitored by a fingertip pulse oximeter (Nonin Onyx 9590 Oximeter) and recorded every 3 minutes.

Statistical analysis

Differences in the time-course changes of the lab parameters will be analyzed by two-way repeated measure ANOVA. If the interaction between groups and time is significant, one-way ANOVA with LSD post hoc test will be used to assess differences between groups at each time point. P values of less than 0.05 will be considered to be statistically significant.

Results

Glucose

The effects of the used treatment parameters gave inconclusive results with no statistically significant difference in glucose levels from one group to the next. All three MES groups were very similar in their trends and outcomes as shown in Figure 4. The control group had an average blood glucose change of 22.08% mg/dL from the initial consumption of the glucose drink to the end of the experiment. The TENS group had an average blood glucose change of 47.76% mg/dL. The Russian group had an average blood glucose change of 21.34% mg/dL. The NMES group had an average blood glucose change of 36.50% mg/dL. Of note was the Russian group, which had the smallest difference between the initial and final glucose level. This represented the greatest blood glucose uptake among the four groups.

Heart Rate

The effects of the established treatment parameters gave unremarkable results with no statistically significant differences in heart rate levels from onset to finish of the experiment for all groups (Figure 5). All groups maintained an average within 55-71 beats per minute without any significant trends throughout the duration of the 90 minute experiment.

Oxygen Consumption (VO2)

The effects of the established treatment parameters gave statistically significant increases in VO2 levels from the Russian group compared to the control. No other statistically significant differences in VO2 were found. Russian and TENS showed the greatest percent increase in VO2 based on 10 minute averages as shown in Figure 6. The control group had an average increase in VO2 of 0.22% from the start of the experiment to the end of the experiment. The TENS group had an average increase in

VO2 of 2.74%. The Russian group had an average increase in VO2 of 5.93%. The NMES group had an average increase in VO2 of 0.03%. Of note was the Russian group, which had the largest average increase in VO2 measurements (10% increase at the peak). This may represent the greatest amount of increased expended energy with Russian.

Discussion

MES on Glucose Levels

The basis for our study was completed under the assumption that, to the best of our knowledge, we were the first group to test multiple parameters of electrical myostimulation while measuring the effects on glucose uptake after a single bout of muscle electrical stimulation. Our literature review identified four recent studies (18, 19, 21, 22) which resulted in successful, statistically significant increases in glucose uptake in skeletal muscle due to single bouts of MES. We have analyzed possible reasons why our study did not result in statistically significant changes in glucose metabolism by comparing the differences between our study and the literatures that resulted in positive evidence.

Our subject populations varied significantly from previous research. Eighteen out of our study's 28 subjects were active females with an average age of 24.94. The majority of the other referenced studies included sedentary males with an average age of 45.01. Males have been hypothesized to have greater glucose uptake and been proven to have a greater number of Type II muscle fibers, which are the muscle fiber type primarily activated in electrical stimulation (22). Additionally, when compared to an active and healthy population, a sedentary population with an existing diagnosis of T2D may have more opportunity for change in glucose values due to greater postprandial glucose fluctuations (25). Therefore, we assume a greater positive result may be seen on older, more sedentary male or even T2D populations.

Our chosen electrode placement included 2 electrodes on the quadriceps and two electrodes on the hamstrings for each lower extremity, for a total of 8 electrodes. Better results may have been observed with recruiting a greater number of muscle fibers by placing electrodes on more muscle groups. Additional muscles utilized in combination with the quadriceps and hamstrings in the other studies included the gluteus muscles (21, 22) tibialis anterior (18), and triceps surae (18). It stands to reason that recruiting a greater number of muscle fibers would have increased the opportunity for glucose uptake in the skeletal muscle.

The amount of time that electrical myostimulation was applied to the subjects for our study was similar to other studies. The variance came in the quantity of time that glucose was measured following the onset of stimulation. Our design took the final glucose reading 60 minutes following the onset of stimulation. All other designs took final measurements either 110 minutes (18, 19) or 120 minutes (21, 22) following the onset of stimulation. As a result, other studies had an additional 50-60 minute allowance for further uptake of glucose to occur.

In this study, the research design utilized a fasting blood glucose protocol outlined by the Centers for Disease Control and Prevention (CDC). The protocol was used to determine each subject's baseline glucose measurement as well as the increase in blood glucose values with ingestion of Trutol®. Two of the other successful studies utilized a set meal of 612 kcal versus the 300 kcal available in the oral glucose drink we chose to use (21, 22). Within the 612 kcal meal, there was a 24% higher content of carbohydrates in comparison to Trutol®. Higher caloric intake, specifically when related to carbohydrates, will result in a greater spike in glucose which then necessitates a higher amount of insulin release and greater change from baseline blood glucose values. Therefore, these previously conducted studies, again, may have demonstrated a greater opportunity for glucose uptake.

Finally, we believe a large degree of our study's variance compared to past studies lies in the quality of equipment used to measure changes in blood glucose throughout the experiment. The aforementioned studies utilized euglycemic clamps to obtain a continuous measurement of intravenous blood insulin values. We were limited by the equipment available to our study without access to glycemic clamps, considered the gold standard for measurement of glucose metabolism (26). The accuracy and sensitivity of our handheld glucometers could have varied based on numerous factors such as the following: hematocrit level, triglyceride level, the temperature and humidity of the room, ingestion of certain drugs including ascorbic acid (27-29).

MES on VO2

A general trend of increased oxygen consumption (VO2) was noted with all applied parameters of electrical stimulation in comparison to the control group. In particular, it was seen that both Russian and TENS applications demonstrated the greatest and most prolonged rise in VO2 levels with Russian protocol causing the greatest and only statistically significant effect on VO2. Two factors including stimulation intensity as well as group characteristics may help to further understand the trend of oxygen consumption.

Generally, an increase in oxygen consumption is expected during progressive exercise with increased workload on the body. Most of the body's energy is produced aerobically, and therefore, VO2 is useful to measure energy expenditure. Additionally, it has also been supported that during low level exercise (defined as being below the lactate threshold (LT)) the body will reach a steady state level of oxygen consumption within 3 minutes from the onset of exercise (30, 31). This concept may help to explain the results of VO2 with our MES. The intensity of Russian and TENS applications may have exceeded the LT, allowing gradual increases in O2 consumption to continue. Meanwhile, the alternative control and NMES groups possibly did not exceed an intensity above the LT resulting in an almost immediate steady state VO2 level that then quickly approached baseline following cessation of interventions. Therefore, it may be theorized that an increased intensity in electrical stimulation would increase the body's workload beyond LT and allow further increases in VO2 for all intervention parameters. This increased intensity may be accomplished by increasing the number of electrodes (and surface area) applied to the subjects. Additionally, an increase in intensity, and possible increase in outcomes, may also be accomplished with increased duration of electric stimulation. One study reporting significantly improved VO2 kinetics following inclusion of electrical myostimulation application included 18 sessions of 30 minutes as opposed to our study consisting of only a single 30 minute application(32).

Another factor that may have affected the results is found in group characteristics. In the current study, the subjects were randomly assigned to one of 4 groups. The resulting groups included 100% female subjects for both the Russian and TENS groups whereas both the control and NMES groups were mixed genders. Some proposed differences in gender that may have impacted the results of this study include differences in lactate threshold and differences in sensitivity to electrical stimulation. One study looked at differences between elite male and female rowers and found a lower LT in female athletes compared to males (33). This would possibly allow a lower level of electrical stimulation to be able to exceed the LT and cause a continued rise in VO2. Another study found that, in general, women exhibit increased sensitivity and decreased inhibition to experimentally induced pain or stimulation as compared to the men (34). This increased response could possibly contribute to increased physiological effects from the applied interventions in the groups comprised solely of female subjects.

An additional factor that may have impacted outcomes between groups that should be considered is the body composition of subjects. Body Mass Index (BMI) was utilized in this study to normalize among subjects. However, some studies recommended normalization using body composition (or fat free mass) as opposed to BMI (35). This could also explain a difference between the gender of the groups as there is typically a difference in the average body composition of males compared to females.

With these possible explanations for the differences in the VO2 results among groups, it should be noted that statistically significant differences in this study were only identified comparing Russian current to the control. However, the additional trends have been identified, discussed, and will require further research for more conclusive outcomes.

Limitations

Our study represented a relatively small sample size of 28 subjects. A trend was identified with this number of subjects, though we recognize that greater trends would have been observed with a much larger sample size. A further limitation that could not be controlled was the fact that data collection required a 2 hour time commitment from the subjects following an 8-hour fast, limiting the number of individuals willing to participate. The smaller subject population with a female majority lacked diversity, despite randomization, and two groups consisted solely of female populations. A more consistent increase in intensity of the electrical stimulation may have been more ideal for this study. We were, however, limited to controlling the intensity based on subject tolerance. The comfort of our subjects was highly prioritized, therefore this was a limitation that was recognized and accepted in the initial design of the study. Additionally, there was a limitation of funds and access to the highest caliber of research equipment, specifically regarding continuous blood glucose measurement.

Future Direction

Future research should be conducted to investigate the effects of various settings of myoelectrical stimulation within a population of subjects with T2D versus a healthy population for both acute and long term effects. More specifically, the VO2 trend noted in our study with the Russian and TENS groups should be further investigated. Further research is suggested to consider the following: increased number of subjects, increased experimental time frame, and increased sensitivity of glucose measurements (continuous glucose monitoring).

Conclusion

There were no other significant changes identified in this experiment resulting from the application of MES to our healthy subjects in regards to changes in postprandial glucose levels and heart rates. Further in-depth research regarding VO2 and glucose changes with application of Russian is recommended based on the positive trends and statistical significance observed in this study.

Figures and Figure Legends

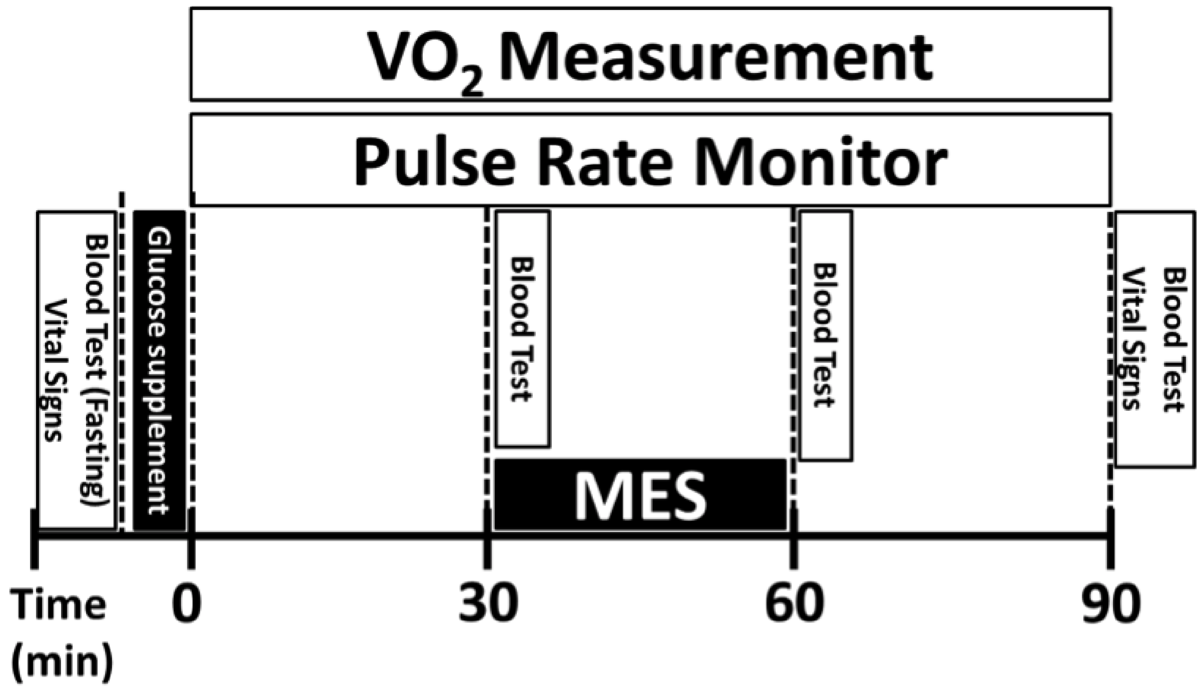

Figure 1. The time frame of research design. VO2: Oxygen Consumption; MES: Motor-level Electrical Stimulation

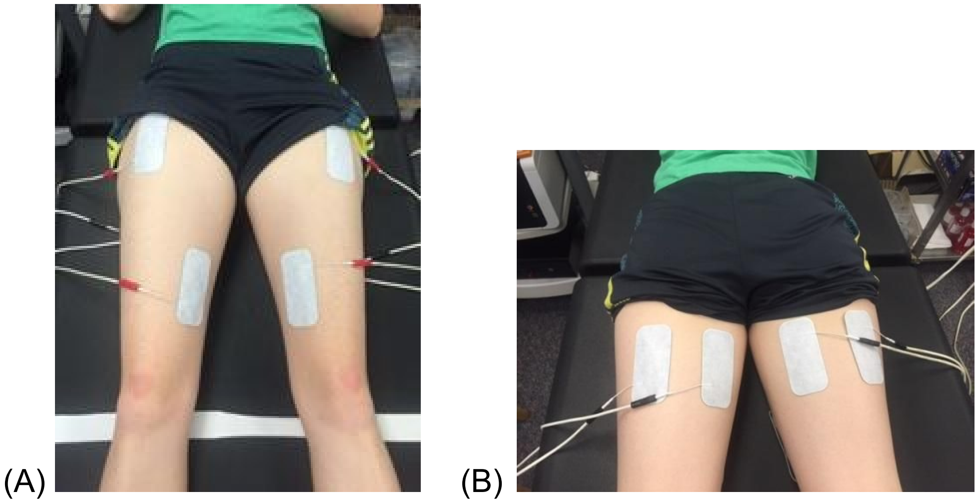

Figure 2. Four pairs of electrodes were applied on each subject. The target muscles on the thigh are the (A) quadriceps and (B) hamstrings.

Figure 3. VO2 mask set-up applied on each subject. Equipment connected to Quark CPET software to analyze VO2 data.

Figure 4. Graphed glucose results. Results for all four groups illustrated. No statistically significant findings were present.

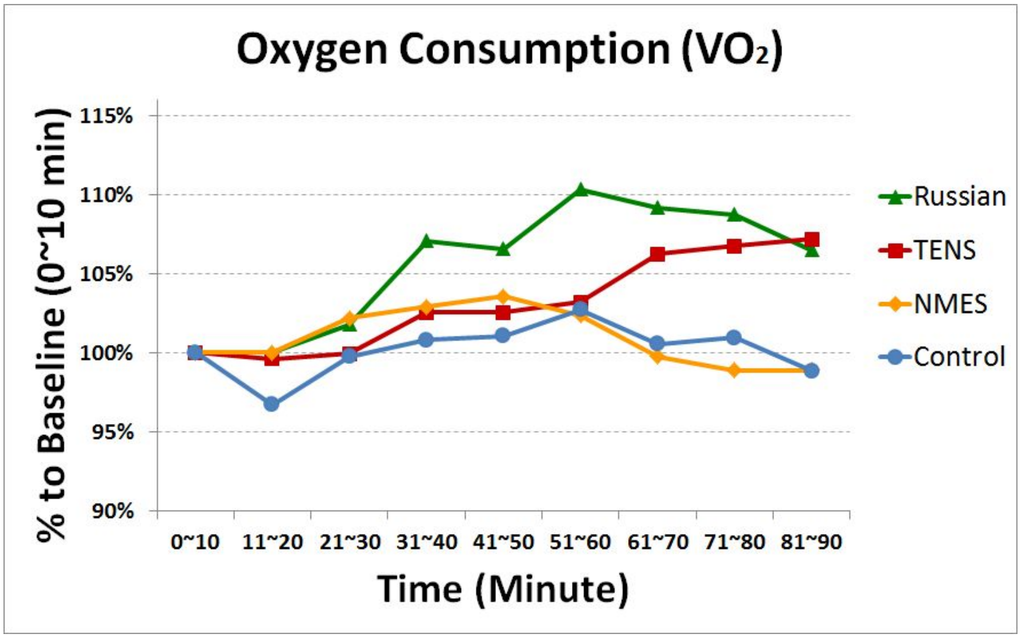

Figure 5. Graphed VO2 results. Results for all four groups illustrated. Statistically significant findings were present in the Russian group. Significant findings were present in the 51-60 minute and 61-70 minute marks for the Russian group.

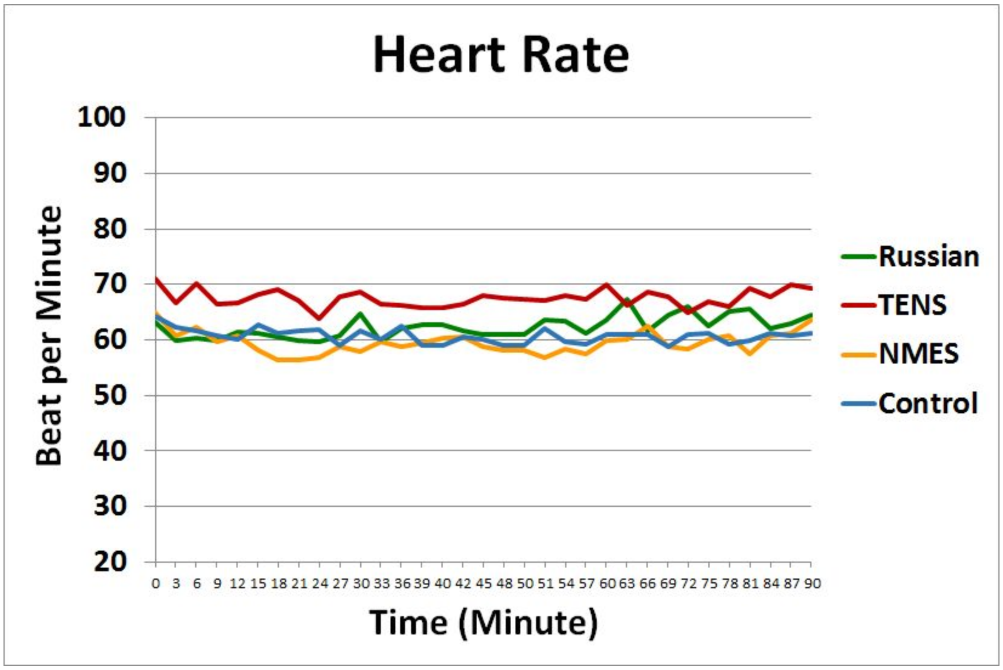

Figure 5. Graphed HR results. Results for all four groups illustrated. No statistically significant findings were present.

	NMES (n=7)	Russian current (n=7)	Low-rate TENS (n=7)	Control (n=7)	P-value
Gender (Male/Female)	6 / 1	0 / 7	0 / 7	4 / 3	NA
Age (years)	25.0 ± 0.9	25.4 ± 1.3	24.0 ± 0.5	25.0 ± 0.5	0.70
Height (cm)	176.4 ± 2.9	169.0 ± 2.7	167.3 ± 1.6	176.0 ± 2.7	0.03
Body mass (kg)	77.8 ± 5.9	64.6 ± 3.7	68.7 ± 2.9	80.4 ± 6.2	0.10
BMI (kg/m^2)	24.9 ± 1.5	22.7 ± 1.6	24.6 ± 1.2	25.9 ± 1.7	0.51
HR (bpm)	62.9 ± 3.6	63.1 ± 2.9	71.1 ± 2.8	64.3 ± 4.5	0.32
SBP(mmHg)	119.9 ± 2.4	114.4 ± 4.7	119.1 ± 2.4	129.4 ± 4.8	0.06
DBP(mmHg)	72.6 ± 2.0	68.0 ± 2.8	70.4 ± 4.3	77.3 ± 3.4	0.24

Table 1. Subjects Characteristics. Values are means ± SE for 7 subjects in each group. BMI: Body mass index; HR: Heart rate; bpm: Beats per minute; SBP: Systolic blood pressure; DPB: Diastolic blood pressure

Groups	Pulse Duration	Frequency / Rate
1) NMES	350 μs	50 Hz
2) Russian current	10 ms burst duration	2,500 Hz
3) Low-rate TENS	250 μs	2 Hz
4) Control	NA	NA

Table 2. The parameters setup of pulse duration and frequency/rate for each group

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